IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	:	
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Curran, *et al.*	:	Art Unit: 1656
	:	
Serial No. 10/078,927	:	Examiner: David Steadman
	:	
Filed: February 19, 2002	:	Atty Docket: SJ-01-0032
	:	
For: Cyclin Dependent Kinase 5 Phosphorylation of Disabled 1 Protein	:	

APPEAL BRIEF PURSUANT TO 37 C.F.R. §1.192

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

This is an Appeal from the Rejection of claims 1, 4-8, 10-11, 13-15, 32 and 35 of the referenced application (published on November 21, 2002 as Pub. No. 2002/0172990) dated May 1, 2006. An Amendment under CRF §§ 1.111 and 1.121 to a non-final Office Action was originally filed on August 23, 2006 in which small portions of the text were missing, and then refiled on October 16, 2006 at the recommendation of the Electronic Business Office. New claims 36 – 40 were added in this Amendment. No action has been issued by the Examiner; however, it is expected the Amendment will be entered. The Notice of Appeal was also filed for this application on August 23, 2006, making this Appeal Brief due on October 23, 2006. A Petition for a one-month extension of time accompanies this Appeal Brief, extending the due date for filing of this Appeal Brief to November 23, 2006.

The fees required under §1.17(c) and the required petition for extension of time for one month for filing this brief and fees therefore are addressed in the accompanying papers.

This brief is transmitted in triplicate in accordance with 37 C.F.R. §1.192(a).

I. REAL PARTY IN INTEREST

The real party in interest in this application is St. Jude Children's Research Hospital by virtue of an assignment executed by both named inventors on February 18, 2002 and recorded in the U.S. Patent Office at Reel/Frame 012919/0525 (4 pages).

II. RELATED APPEALS AND INTERFERENCES

No other appeals or interferences are known to appellant, appellant's legal representative, or assignee St. Jude Children's Research Hospital which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

There are a total of 40 claims in this application. Claims 2-3, 9, 12,16-31 and 33-34 have been canceled. Claims 1, 4-8, 10-11, 13-15, 32 and 35 are pending and stand rejected. New claims 36-40 were added in the Amendment filed August 23, 2006 after numerous attempts by the Appellants to modify the claims based on rejections of the Examiner failed to further prosecution. New claims 36 – 40 are broad claims similar to claims previously rejected by the Examiner. These prior rejections are addressed herein based on the assumption that they will be applied by the Examiner to these new claims. No claims have been allowed.

Claims 1, 4-8, 10-11, 13-15, 32 and 35 - 40 are on appeal. The claims on appeal are reproduced in their present form in the attached appendix.

IV. STATUS OF AMENDMENTS

An amendment to an outstanding non-final Office Action mailed May 1, 2006 was filed on August 23, 2006 and then refiled on October 16, 2006 when it was discovered that small portions of the text were missing. This Amendment has yet to be officially entered by the Examiner, but

Appellants expect it to be entered and have incorporated it into the claims appearing in the attached appendix.

V. SUMMARY OF INVENTION

The present invention is based on the discovery that the Disabled 1 protein (Dab1) is a substrate for cyclin-dependent kinase (Cdk5) activity, and is selectively phosphorylated by Cdk5 in vivo. Based on this discovery, an assay to determine Cdk5 activity by detection of Dab1 phosphorylation is provided. The assay is based on the identification of two serine amino acids in Dab1 that are selectively phosphorylated by Cdk5, serine 491 or 515, particularly serine 491.

VI. ISSUES

The following issues remain:

1) Whether Claims 36 – 38 are properly rejected under 35 U.S.C. §112, first and second paragraphs in prior office actions for recitation of "Cdk5" and "Dab1" as being unclear.
2) Whether Claims 36 - 38 were properly rejected under 35 U.S.C. §112, first paragraph in prior office actions for failure to describe a sufficient number of species to recite a genus.
3) Whether Claims 36, 38 and 40 were properly rejected under 35 U.S.C. §112, second paragraph in prior office actions for the term "candidate sequence" being indefinite.
4) Whether Claim 39 was properly rejected under 35 U.S.C. §112, second paragraph in prior office actions as being indefinite for containing genbank accession numbers.

5) Whether Claim 40 was properly rejected under 35 U.S.C. §112, first paragraph in prior office actions for inserting new matter into the disclosure for use of SEQ ID NO:3 as a structural limitation.
6) Whether the amendment filed on April 25, 2005 is properly objected to under 35 U.S.C. §132(a), for introducing new matter into the disclosure of the invention and introducing the alleged new matter into the claims, thus necessitating their rejection on this ground.
7) Whether claims 1, 4-8, 10-11, 13-15, 32 and 35 are properly rejected under 35 U.S.C. §112, first paragraph for failure to comply with the written description requirement.

VII. GROUPING OF CLAIMS

1) Claims 1, 4-8, 10-11, 13-15, 32 and 35 stand or fall together based on the objection for introducing new matter into the specification and the rejection for failure to comply with the written description requirement.
2) Claims 36 and 38 stand or fall together based on the rejections for recitation of "Cdk5" and "Dab1" as being unclear, failure to describe a sufficient number of species to recite a genus and the term "candidate sequence" being indefinite.
3) Claim 37 stands or falls alone based on the rejection for recitation of "Cdk5" and "Dab1" as being unclear and failure to describe a sufficient number of species to recite a genus.
4) Claim 39 stands or falls alone based on the rejection as being indefinite for containing genbank accession numbers.
5) Claim 40 stands or falls alone based on the rejections for the term "candidate sequence" being indefinite and inserting new matter into the disclosure for use of SEQ ID NO:3 as a structural limitation of Dab1.

VIII. ARGUMENTS

A. The terms Cdk5 and Dab1 were well known in the art at the time the present application was filed and adequately describe the invention.

Examiner's Arguments

Throughout prosecution of the present application, the Examiner rejected claims reciting the terms "Cdk5" and "Dab1", now represented by Claims 36 – 38, under 35 USC § 112, first and second paragraphs asserting that these terms are unclear. The Examiner has stated that there is no "clear definition" of the terms "Cdk5" and "Dab1" in the specification and even though these terms may have been used in the art at the time of the invention, the definitions of the terms in the specification are not limited to those "Cdk5" and "Dab1" polypeptides that were known in the art at the time of the invention including genbank accession numbers 3288851 and 1771281. The Examiner stated that the specification fails to define which of the Dab1 and Cdk5 properties are necessary for inclusion of a cyclin-dependent kinase or a disabled-1 protein which is distinct in sequence from similar proteins that may share these characteristics.

Even though the Examiner acknowledged that Dab1 and Cdk5 were known in the art at the time of filing of the invention and further acknowledged that the claims were not drawn to the Dab1 or Cdk5 polypeptides themselves, he asserted that the terms must be limited to particular sequences to meet the requirement of definiteness.

Appellants' Arguments

There is a strong presumption that an adequate written description of the claimed invention is present in the specification. *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (Ct. Cust. Pat. App. 1976); *see also* Manual of Patent Examining Procedure (MPEP) Sec. 2163, page 156, col. 1. To overcome this presumption, the Examiner bears the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. *In re Wertheim*, 541 F2d at 263-

264; *see also* MPEP Sec. 2163, page 158, col. 2. Appellants do not believe the Examiner has met this burden in this case for the reasons set forth below and in the responses submitted December 13, 2004; April 25, 2005 and June 16, 2005.

The terms "Cdk5" and "Dab 1" were well known in the art as of the application filing date of February 19, 2002 and are described in the specification in a manner consistent with these meanings. The specification defines "Cdk5" as "a protein with serine/threonine kinase activity that is structurally homologous to the mitotic cyclin dependent kinases"(p. 4) and defines "Dab1" as "an intracellular adapter protein that is phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity" (p. 4), Appellants also include genbank accession numbers for human and mouse in the definition of Dab1 and human, mouse and rat genbank accession numbers for Cdk5. Appellants also included numerous references in the specification and during prosecution showing prior scientific publications that describe properties of Dab1 and Cdk5 which distinguish them from other cyclin dependent kinases and closely related Dab proteins.

These terms are in fact creations of the art used to denote, in each case, a class of proteins with a unique set of features that allowed them to be grouped together and distinguished from other proteins, even those that are closely related. Furthermore, Dr. Thomas Curran, a co-inventor of the present application and a person of skill in the art provided an expert declaration stating that "Cdk5", "Dab1" and "Cdk5 serine kinase activity" were well known terms in the art at the time the application was filed (see response filed April 25, 2005). Because these terms were well known in the prior art, an exhaustive description does not need to be reproduced in the specification and in fact is preferably omitted according to *Hybritech, Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986.)

Appellants do not rely upon the primary structure; i.e. the amino acid sequence, of any of these proteins to impart patentability upon the claimed compositions. Instead Appellants properly rely on the knowledge of these structures to supplement the description of the novel and unobvious aspects of the invention in the specification. Recitation of the primary structure of

each member of this group of proteins would be redundant to knowledge available in the prior art and is not necessary.

The invention is based on the discovery that Dab1 is specifically phosphorylated by Cdk5. Cdk5 activity is tightly controlled by its regulator, p35, making Cdk5 activity difficult to determine based on levels of Cdk5 present. Furthermore, a substrate which is selectively phosphorylated by Cdk5 had not heretofore been identified. The discovery that Dab1 is specifically phosphorylated on serine within a preferred candidate sequence by Cdk5 is the basis for the invention. The invention is not based on the novelty or nonobviousness of Cdk5 or Dab1, but rather on the special relationship between the two as taught for the first time in the present application. The invention claimed in the present application is directed to a unique method for determining Cdk5 serine kinase activity based on this special relationship.

In *Falkner v. Inglis*, ---F.3d---, 2006 WL 1453040, Slip No. 05-1324 (Fed. Cir. May 26, 2006) the Court of Appeals for the Federal Circuit (CAFC) agreed with the Board of Patent Appeals and Interferences (BPAI) that the poxvirus-based vaccines described in the Inglis applications were adequately described and enabled even though the specification contained no poxvirus sequences or specific examples for making a poxvirus vaccine or the phrase "incorporated by reference". Likewise, in *Capon et al. v. Eshar et al.*, Nos. 03-14480, 1481 (Fed. Cir. August 12, 2005), the CAFC reversed the BPAI and found that claims to chimeric genes composed of pieces of known genes did not need to recite the known gene sequences to satisfy the written description requirement.

As Appellants have argued in the present case regarding the incorporation of "Dab1" and "Cdk5" sequences, the CAFC found that at the time of filing of the earliest Inglis application, the poxvirus genome was well known to those of ordinary skill in the art as evidenced by publication of the genome in professional journals. In view of the well known nature of the poxvirus genome, neither the BPAI or the CAFC found it necessary for the applicant to incorporate the well known poxvirus genome into the specification by reference or otherwise. Indeed, the CAFC

noted that omission of such redundant information from the specification is preferred, reiterating the familiar adage that "[a] patent need not teach, and preferably omits, what is well known in the art." citing *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987). The terms "Dab 1" and "Cdk5" were well known in the art at the time the present application was filed and, according to the reasoning used by the CAFC in *Falkner v Inglis* and *Capon v Eshar*, adequately describe the invention in compliance with 35 U.S.C. §112, first and second paragraphs. Therefore, Appellants respectfully submit that previous rejections made under 35 USC § 112, first and second paragraphs are improper and should not be applied to new claims 36 - 38.

B. The disclosed species are representative of the entire genus

Examiner's Arguments

In prior Office Actions, the Examiner rejected claims under 35 U.S.C. § 112, first paragraph for failure to describe a sufficient number of species to recite a genus for Cdk5 or Dab1. The Examiner asserted that the genera encompass widely variant species with respect to structure and that the three genbank nos. provided for Cdk5 and two genbank nos. provided for Dab1 were insufficient representatives of the genus. The Examiner asserted that other than the two representative species of Dab1 polypeptides, the specification failed to disclose any other additional representative species of the genus. The Examiner maintained that the disclosure of the two representative species of Dab1 polypeptides is insufficient to be representative of the attributes and features of all species encompassed by the recited genus of Dab1 polypeptides.

The Examiner maintained that the alleged novel relationship claimed by Appellants, i.e., the phosphorylation of Dab1 by Cdk5, has not been shown in all organisms that express "Cdk5" and "Dab1" polypeptides. The Examiner asserted that there is no disclosure in the specification or in the prior art of a structure-function correlation between the members of the respective genus

of Cdk5 or Dab1 polypeptides such that by the mere recitation of "Cdk5" or "Dab1" one of skill can visualize the structures of all members of the respective genus.

Appellants' Arguments

"Any assertion by the Patent Office that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasons substantiating the doubts so expressed." *In re Dinh-Nguten and Stenhagen*, 181 USPQ 46, 47 (Ct. Cust. & Pat. App. 1974); *see also In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Armbruster*, 185 USPQ 152, 153 (Ct. Cust. & Pat. App. 1975); *In re Bowen*, 181 USPQ 48 (Ct. Cust. & Pat. App. 1974); *In re Hawkins*, 179 USPQ 157, 162 (Ct. Cust. & Pat. App. 1973). Even at the request of Appellants throughout prosecution, the Examiner provided no scientific rational or evidentiary support for the assertion that the disclosed Cdk5/Dab1 relationship is peculiar to a single species. In the absence of such support, Appellants submit that the Examiner has failed to carry his burden for establishing prima facie nonenablement.

Even though this rejection does not need to be affirmatively rebutted because it is not supported by any evidence or reasoning, Appelants have explained the enabling nature of the disclosure for all species that harbor Cdk5 and Dab1 proteins. Example 1 of the specification provides results obtained in a mouse model, which show Cdk5 specifically phosphorylates Dab1 at serine 491. Appellants provided evidence showing Dab1 phosphorylation on serine 491 is Cdk5 activity-dependent in a rat model as well. Appellants also provided sequence alignments for mouse, rat and human Cdk5 and Dab1 (which were all in the public domain at the time the present application was filed) showing that both proteins are highly conserved among the three species. Appellants also showed the Dab1 sequence alignment between mouse and human is 96% identical, mouse and dog is 90% identical, mouse and bird is 89% identical, mouse and cow is 84% identical and mouse and zebrafish is 66% identical.

Appellants have provided examples for two representative species and have provided support showing that Dab1 and Cdk5 are highly conserved proteins in many different species. In

Falkner v. Inglis, ---F.3d---, 2006 WL 1453040, Slip No. 05-1324 (Fed. Cir. May 26, 2006) the CAFS states:

> A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation.

The specification in the Inglis application focused on herpesvirus; it did not show specific examples of the claimed invention as it related to a poxvirus. However, the CAFS held that a person skilled in the art was capable of taking the claimed invention and applying it to a poxvirus. Likewise, a person of skill in the art, would have been able to identify a Dab1 and Cdk5 protein from any desired species and determine if Dab1 was phosphorylated on a serine within a preferred sequence as taught in the present application.

Having shown examples of how specific Dab1 phosphorylation can be used as a proxy for Cdk5 activity in representative species, and showing these proteins are highly conserved among species, Appellants submit that one of skill in the art would have no problem using this method to detect the activity of any Cdk5 within other species. Accordingly, Appellants respectfully submit that previous rejections made under 35 U.S.C. § 112, first paragraph for failure to describe a sufficient number of species were improper and should not be applied to new claims 36 - 38.

C. The term "preferred sequence" is definite

Examiner's Arguments

The Examiner rejected prior claims for use of the term "candidate sequence preferred by cdk5 activity" under 35 U.S.C. 112, second paragraph as being indefinite. The Examiner acknowledged the definition of the term "candidate sequence" at page 5 of the specification.

However, the Examiner asserted this definition provides no indication as to the scope of those candidate sequences that are "preferred" by a "cdk5 activity" and that the term remained indefinite. The Examiner maintained that this term is indefinite in view of the indefiniteness of the term "cdk5 activity" and that the scope of candidate sequences are those that are "preferred" by cdk5 activity. It is unclear from the specification and the claims as to whether all sequences that have a serine followed by proline at the +1 position and a lysine in the +3 position are those that are "preferred" by a "Cdk5 activity" or whether only a subset of those sequences that have a serine followed by proline at the +1 position and a lysine in the +3 position are meant to be encompassed as being sequences that are "preferred" by "cdk5 activity."

Appellants' Arguments

Appellants maintain that the specification specifically defines a "candidate sequence" as a sequence of amino acids which contains a serine followed by a proline in the +1 position and a lysine in the +3 position, the serine being a preferred site for Cdk5 activity (Songyanget al., Mol Cell Biol, 16:6486-6493, 1996). Songyang et al. teach that this sequence is a distinct optimal peptide substrate for the Cdk5 kinase. Furthermore, on page 20 lines 8-18 of the specification, Appellants predicted murine Dab1 serines 491 and 515 to be Cdk5 phosphorylation sites based on sequence analysis and then conducted experiments to show their prediction was true.

Appellants have shown the terms "Cdk5" and "Dab1" were well defined and were well known by a person of skill in the art at the time of filing. Dr. Thomas Curran, a co-inventor of the present application and a person of skill in the art stated in his expert declaration filed in the April 25, 2005 response that "Cdk5 serine kinase activity" was well understood and used extensively in the art at the time the application was filed. It was well known in the art that serine kinase activity refers to the ability of a protein (in this case Cdk5) to phosphorylate a serine. A person of skill in the art knows the meaning of "cdk5 serine kinase activity" and the specification defines what constitutes a candidate sequence in a manner that allows a skilled artisan to routinely identify such sequences. Appellants discuss the definition of a candidate sequence and

show how they determined that the serines within the two candidate sequences found in the carboxy terminal domain of Dab1 were phosphorylated by cdk5 serine kinase activity.

Appellants respectfully submit that rejections made under 35 USC § 112, second paragraph were improper and should not be applied to the use of the term "candidate sequence" in Claims 36, 38 and 40.

D. Genbank accession numbers are definite

Examiner's Arguments

The Examiner rejected previous claims containing genbank accession numbers as being indefinite. The Examiner asserted that it is well known to one of skill in the art that sequence accession numbers are updated by modifying the sequence of a particular accession number. The Examiner stated that there is no way to know with certainty that the sequence of genbank accession numbers will not change. Genbank accession numbers are not static, but can change by revision. The Examiner provided an example of the revision history for Accession Number X761041 (a protein unrelated to this application).

Appellants' Arguments

The U.S. Patent Office has previously accepted the use of genbank accession numbers in claims to refer to biological sequence information known and available in the prior art. For example, U.S. Patent No. 6,770,742, issued August 3, 2004 claims a fibroblast growth factor receptor-4 by reference to a genbank accession number. The FGFR-4 sequence is not listed in the sequence listing, thus there is no SEQ ID qualifier for the FGFR-4 receptor. Furthermore, the revision history for this genbank accession number shows that it was revised no less than 7 times. Additional granted patents in which the patentee was allowed to refer to nucleotide or amino acid sequences according to genbank numbers in the claims include, but are not necessarily limited to, U.S. Patent Nos. 6,949,342; 6,943,006; 6,890,572 and 6,667,065.

Since there appears to be no per se rule against the use of genbank accession numbers in claims, Appellants ask that the use of genbank numbers be allowed in this instance where the sequence itself does not go to the heart of the invention, but is simply useful information for understanding the invention.

In a copy of the revision history for Accession Number X761041 provided by the Examiner in the Office Action dated August 22, 2005, each date the accession number was revised is clearly shown. Furthermore, a link is provided so that one can review the contents of the accession number for each date prior to a revision. Since a person of skill in the art knows the filing date of the present application, that person can easily access the sequence in genbank that was known at that time. Therefore, the use of genbank accession numbers in the claims is clear and definite. Furthermore, any changes that might be made to this sequence would not be expected to change the characteristics of the Cdk5 or Dab1 proteins which are important in the context of the claimed invention.

Appellants respectfully submit that rejections made under 35 USC § 112, second paragraph, based on the assertion that the use of genbank numbers renders the claims indefinite, are improper and should not be applied to Claim 39.

E. The use of SEQ ID NO:3 as a structural limitation is not new matter

Examiner's Arguments

In an attempt to address the Examiner's rejection of previous claims stating that a genus requires a precise definition, such as structure, formula or chemical name of the claimed subject matter to sufficiently distinguish it from other materials, Appellants amended the claims to require that the Dab1 protein include SEQ ID NO:3. Support for SEQ ID NO:3 can be found on page 3, lines 25 – 29 and page 15, lines 16-17.

The Examiner rejected the claims that incorporated SEQ ID NO:3 as a structural limitation for Dab1 proteins under 35 U.S.C. 112, first paragraph for inserting new matter. The

Examiner asserted that while the disclosure provides support for the peptide of SEQ ID NO:3, it fails to support the recited genus of Dab1 polypeptides comprising SEQ ID NO:3. The Examiner maintained that while all members of the genus of Dab1 polypeptides comprise the structural feature of the 14 amino acid peptide of SEQ ID NO:3, this structural feature does not constitute a "substantial portion" of the genus of recited Dab1 polypeptides. Thus, the Examiner maintained the specification failed to adequately describe the claimed invention.

Appellants' Arguments

SEQ ID NO:3 comprises 14 amino acids found in the c-terminal portion of the Dab1 protein in several different species including mice, rats, humans, birds, dogs and cows. Proteins other than Dab1, even closely related proteins such as Dab2, do not share this sequence. SEQ ID NO:3 is provided as a common structural reference for the genus of Dab1 proteins to supplement the distinguishing features of Dab1 noted in the specification. A peptide having the sequence of SEQ ID NO:3, as shown in the specification, was used as an antigen to generate an antibody that binds to Dab1. The use of this peptide as an antigen reveals to one of skill in the art that this is a sequence that is characteristic of Dab 1 and useful for distinguishing Dab1 from other proteins. Therefore, inclusion of SEQ ID NO:3 in the claims as a feature of Dab 1 is fully supported by the specification and is not new matter.

Appellants respectfully submit that the rejection made under 35 U.S.C. § 112, first paragraph, for inserting new matter, should not be applied to Claim 40.

F. Introducing sequence information based on genbank accession numbers found in the specification without the words "incorporated by reference" specifically stated in the specification is not introducing new matter

The Examiner objected to the amendment filed April 25, 2005 under 35 U.S.C. 132(a) for introducing new matter into the disclosure. The Examiner asserts that according to MPEP § 608.01(p) incorporation by reference of material in a non-patent document "must be set forth in

the specification and must: (1) Express a clear intent to incorporate by reference by using the root words "incorporat(e)" and "reference" (e.g., "incorporate by reference"); and (2) Clearly identify the referenced patent, application, or publication." See 37 § 1.57(b). Furthermore the Examiner states that MPEP § 608.01(p) further states, "[i]f a reference to a document does not clearly indicate an intended incorporation by reference, examination will proceed as if no incorporation by reference statement has been made and the Office will not expend resources trying to determine if an incorporation by reference was intended."

The Examiner rejected Claims 1, 4-8, 10-11, 13-15, 32 and 35 as failing to comply with the written description requirement. The Examiner asserts that the claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Prior to making the present objection and rejection, the Examiner previously determined that SEQ ID NOs: 4 and 5 were intended to be incorporated by reference based on the inclusion of the appropriate genbank numbers. The Examiner withdrew an objection in the August 22, 2005 Office Action, stating that the disclosed GenBank Accession Number in the specification is considered to be an inherent "incorporation by reference", and proceeded to examine the claims based on the inclusion of SEQ ID NO:4 (mouse Dab1). On page 9 of the Office Action dated February 21, 2006, the Examiner allowed a claim that incorporated SEQ ID NO:4 and indicated that 2 other claims, one that incorporated SEQ ID NO:4 and another that incorporated SEQ ID NO:5, would be allowed if written in independent form. However, in the Office Action dated May 1, 2006, the Examiner reconsidered this determination and rejected the claims citing 37 C.F.R.§1.57 and MPEP § 608.01(p). The Examiner asserted the originally filed disclosure does not provide support for SEQ ID NO:4 and SEQ ID NO:5 which are included in Claims 1, 32 and 35 based on the fact that the root words "incorporate" and "reference" do not appear in the specification. According to the Examiner, even though the genbank accession numbers are

included in the definition of Dab1, this is insufficient support for incorporating the sequences associated with these accession numbers (i.e. SEQ ID Nos. 4 and 5) because the specification does not specifically state the accession numbers are to be incorporated by reference.

Appellants respectfully disagree with the preceding objection and rejection of the Claims. The regulation cited to support this rejection, 37 C.F.R.§1.57, was added on Sept. 21, 2004 and became effective Oct. 21, 2004, well after the February 19, 2002 filing date of the present application. Furthermore, MPEP § 608.01(p) was not amended until Oct. 21, 2004 to include the language stated in the above objection by the Examiner. A patent application should not be faulted for failing to adhere to rules established well after its filing date.

However, even if Appellants are held to this standard, 37 C.F.R. § 1.57 (g)(1) does allow correction to comply with paragraph (b)(1) of this section if the application as filed clearly conveys an intent to incorporate the material by reference. 37 C.F.R. § 1.57 (g)(2) states that [a] correction to comply with paragraph (b)(2) of this section is permitted for material that was sufficiently described to uniquely identify the document.

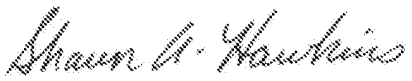
On page 4, lines 24-25 of the specification, Appellants specifically define Dab1 proteins as including proteins cloned from genbank accession numbers 3288851 and 1771281. As Appellants argued earlier in its response dated June 16, 2005 to the Examiner's assertion made in the Advisory Action mailed May 18, 2005, including these genbank numbers as part of the definition of Dab1 reflects Appellants' intent for these publications to be incorporated by reference. Appellants also indicated during prosecution that the sequences incorporated into the specification were the sequences found in the genbank accession numbers at the time of filing of the application. Thus, Appellants have fulfilled the requirements of 37 § 1.57 (g)(1) and (g)(2).

In light of the arguments presented above, Appellants have overcome the objection and rejection of Claims 1, 4-8, 10-11, 13-15, 32 and 35.

VIII. Conclusion

For the foregoing reasons, Appellants believe that the Examiner's rejections of Claims 1, 4-8, 10-11, 13-15, 32 and 35 – 40 are erroneous and reversal of all outstanding rejections is therefore respectfully requested.

Respectfully submitted,



Shawn Annette Hawkins
Agent for Appellants
Registration No. 50,318

St. Jude Children's Research Hospital
332 North Lauderdale
Memphis, TN 38105-2794
Telephone: 901-495-2751

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APPENDIX OF CLAIMS INVOLVED IN THIS APPEAL

Claim 1 A method for detecting cyclin dependent kinase 5 (Cdk5) serine kinase activity in a biological sample, which method comprises determining whether Disabled 1 protein (Dab1) in said sample is phosphorylated on a serine selected from the group consisting of a serine at position 491 of the polypeptide encoded by SEQ ID NO:4 or SEQ ID NO:5 and a serine at position 515 of the polypeptide encoded by SEQ ID NO:4 or SEQ ID NO:5, wherein phosphorylation of Dab1 on said serine indicates the presence of active Cdk5 in said sample.

Claim 4 The method of claim 1 wherein said biological sample is isolated from an organism selected from the group consisting of mouse and human.

Claim 5 The method of claim 1 wherein said biological sample is isolated from the group consisting of brain and blood.

Claim 6 The method of claim 1 wherein said biological sample is isolated from a cell culture.

Claim 7 The method of claim 1 wherein said Dab1 phosphorylation occurs *in vivo*.

Claim 8 The method of claim 1 which comprises immunoprecipitating said Dab1 from said biological sample prior to said determining step using an antibody that binds to Dab1 phosphorylated and unphosphorylated on said serine.

Claim 10 The method of claim 1 wherein Dab1 phosphorylation is determined using an antibody that binds to Dab1 only when it is phosphorylated on said serine.

Claim 11 The method of claim 10 wherein said antibody is raised against the polypeptide fragment TPAPRQSS(PO_4)PSKSSA (SEQ ID NO:3 which contains a phosphate group on the 8th amino acid).

Claim 13 The method of claim 10 wherein said antibody is polyclonal.

Claim 14 The method of claim 10 wherein said antibody is monoclonal.

Claim 15 The method of claim 10 wherein Dab1 phosphorylation is determined by using techniques consisting of radioimmunoassay, ELISA, "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays, western blots, precipitation reactions, agglutination assays, complement fixation assays, immunofluorescence assays, protein A assays, immunoelectrophoresis assays, mass spectrometry and antibody array.

Claim 32 A method for detecting cyclin dependent kinase 5 (Cdk5) serine kinase activity in a biological sample, which method comprises immunoprecipitation of mouse Dab1 encoded by the sequence set forth in SEQ ID NO:4 from said biological sample; contacting the immunoprecipitated Dab1 with a phosphoantibody generated using SEQ ID NO:3 having a phosphorylated serine at position 8 of SEQ ID NO:3 as an antigen; detecting binding of the phosphoantibody to serine 491 of said Dab1, wherein binding of the phosphoantibody to serine 491 of said Dab1 in such biological sample indicates the presence of Cdk5 serine kinase activity in said sample.

Claim 35 A method for detecting cyclin dependent kinase 5 (Cdk5) serine kinase activity in a biological sample, which method comprises immunoprecipitation of human Dab1 encoded by the sequence set forth in SEQ ID NO:5 from said biological sample; contacting the immunoprecipitated Dab1 with a phosphoantibody generated using SEQ ID NO:3 having a phosphorylated serine at position 8 of SEQ ID NO:3 as an antigen; detecting binding of the phosphoantibody to serine 491 of said Dab1, wherein binding of the phosphoantibody to serine 491 of said Dab1 in such biological sample indicates the presence of Cdk5 serine kinase activity in said sample.

Claim 36 A method for detecting cyclin dependent kinase 5 (Cdk5) serine kinase activity in a biological sample, which method comprises determining whether the carboxy

terminal domain of Disabled 1 protein (Dab1) in said sample is phosphorylated on a serine within a candidate sequence preferred by cdk5 activity, wherein phosphorylation of Dab1 on said serine indicates the presence of active Cdk5 in said sample.

Claim 37 The method of claim 36 wherein said serine is selected from the group consisting of a serine corresponding to position 3 of QSSPSK (SEQ ID NO:1), such position being determined by alignment of Dab1 with reference to amino acid positions of SEQ ID NO:1 and a serine at position 21 of SSASHVSDPTADDIFEEGFESPSK (SEQ ID NO:2), such position being determined by alignment of Dab1 with reference to amino acid positions of SEQ ID NO:2.

Claim 38 A method for detecting cyclin dependent kinase 5 (Cdk5) serine kinase activity in a biological sample, which method comprises immunoprecipitation of Dab1 from said biological sample; contacting the immunoprecipitated Dab1 with a phosphoantibody generated using SEQ ID NO:3 having a phosphorylated serine at position 8 of SEQ ID NO:3 as an antigen; detecting binding of the phosphoantibody to a serine within a candidate sequence preferred by cdk5 activity in the carboxy terminal domain of said Dab1, wherein binding of the phosphoantibody to said serine of said Dab1 in such biological sample indicates the presence of Cdk5 serine kinase activity in said sample.

Claim 39 A method for detecting cyclin dependent kinase 5 (Cdk5) serine kinase activity in a biological sample, which method comprises determining whether Disabled 1 protein (Dab1) in said sample is phosphorylated on a serine selected from the group consisting of a serine corresponding to position 491 of the amino acid sequence encoded by the nucleotide sequence of GenBank Accession number 1771281 and a serine corresponding to position 515 of the amino acid sequence encoded by the nucleotide sequence of GenBank Accession number 1771281,

wherein phosphorylation of Dab1 on said serine indicates the presence of active Cdk5 in said sample.

Claim 40. A method for detecting cyclin dependent kinase 5 (Cdk5) serine kinase activity in a biological sample, which method comprises determining whether the carboxy terminal domain of Disabled 1 (Dab1) protein comprising SEQ ID NO:3 in said sample is phosphorylated on a serine within a candidate sequence preferred by cdk5 kinase activity, wherein phosphorylation of Dab1 on said serine indicates the presence of active Cdk5 in said sample.